Research Article

Seroprevalence of Scrub Typhus, its Current Epidemiological Trend and Clinical Manifestation in Eastern India: Insights from Endemic Regions

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ABSTRACT

Objectives: Scrub typhus caused by *Orientia tsutsugamushi* represents a notable public health concern across India, particularly in Odisha. Since the symptoms are not specific, there is a need for a definitive and comprehensive diagnostic evaluation. The primary objective of this investigation was to establish a firm groundwork for further analysis, underscoring the escalating importance of scrub typhus as a major health hazard in the eastern region of India.

Materials and Methods: A retrospective cross-sectional analysis was conducted from April 2023 to March 2024, and it included 3,579 patients presenting with acute febrile illness at IMS and SUM Hospital, Bhubaneswar. Laboratory data of serological assessment using the InBios Scrub typhus IgM kit was obtained and analyzed to identify seropositive scrub typhus cases. The data was assessed utilizing Epi-Info software (version 3.5.1, Centre for Disease Control and Prevention, Atlanta, GA, USA).

Result: Out of 3579 serum samples, 235 (6.79%) were scrub typhus positive, mostly presenting with non-specific symptoms such as fever (100%) and dermatological eruptions (20%). The majority belonged to the 21-40 age group (31.49%). An intriguing transition from rural to urban settings was discerned. Organ-specific symptoms included polyarthralgia (97;41.28%), lymphadenopathy (70;30.21%), and hepatomegaly (35;14.89%), whereas eschar was rarely (6;2.55%) observed. A marked seasonal variation was evident, with its peak incidence during the monsoon season (178;10.91%).

Conclusion: This investigation accentuates the escalating significance of scrub typhus as a public health concern in eastern India, emphasizing the necessity for sustained research initiatives and enhanced public health interventions to manage efficiently.

Keywords: Orientia tsutsugamushi, IgM ELISA, Acute febrile illness, Eschar, Monsoon season

1. INTRODUCTION

In eastern India's widespread and diverse ecosystems, *O. tsutsugamushi*, the causative agent of scrub typhus, prospers quietly among the abundant vegetation and rich biodiversity. Despite its low prevalence, this bacterium holds considerable influence on the welfare and health of populations throughout the area, posing a substantial obstruction to healthcare management. Studies reveal that it affects both genders, with a higher prevalence in males, and commonly impacts individuals aged between 46-60. The disease is no longer confined to the rural arena, showing an urbanised trend [1].

Clinical manifestations include fever, headache, rash, lymphadenopathy, and fatal complications like encephalitis and acute respiratory distress syndrome (ARDS). The absence of characteristic eschar features makes these cases difficult to detect [1-3]. In rural southern India, the seroprevalence among febrile patients is approximately 19.2%, whereas specific areas in China document rates as elevated as 40-50%. Thailand also exhibits a high seroprevalence, with percentages ranging between 15%-23% in diverse localities. Seasonal variations,

occupational exposure, and regional ecology influence these distinctions. Epidemiologically, scrub typhus is defined by its transmission through chiggers of the genus "Leptotrombidium," by small mammals, particularly rodents, acting as natural reservoirs [4, 5]. The diagnosis mostly depends on serological testing**,** including the indirect immunofluorescence assay (IFA), IgM/IgG ELISA, and recently developed rapid diagnostic tests (RDTs). With limited access to molecular settings like PCR in resource-constrained areas and peripheral setups, IgM ELISA remains a reliable diagnostic assay for the routine testing of scrub typhus. A recent or past infection can be detected by detecting specialised antibodies (IgM or IgG) against the scrub typhus group. Multiple immunoassays have been created to identify these specific IgM antibodies, utilizing whole blood cells or genetically engineered antigens. Identifying IgM antibodies against various strains of *O. tsutsugamushi* in the initial stage of infection suggests an ongoing acute infection [6]. Prompt treatment with antibiotics like doxycycline or azithromycin is crucial for a favourable outcome. Scrub typhus outbreaks have been successfully contained through chemoprophylaxis and appropriate protective measures [7]. Careful correlation with the clinical symptoms, timely identification, and proper management are imperative in alleviating the morbidity and mortality linked with scrub typhus. The re-emergence of scrub typhus in areas not endemic earlier highlights the need for sustained research endeavours and improved public health strategies to manage and control this resurging infectious disease. This study aimed to establish a firm groundwork for further investigation and intervention planning, underscoring the escalating importance of scrub typhus as a public health issue in the eastern region of India.

2. MATERIAL AND METHODS

Study design

A cross-sectional descriptive/epidemiological study was conducted retrospectively for one year, from April 2023 to March 2024, in the Department of Microbiology at the Institute of Medical & SUM Hospital, Bhubaneswar. All serum samples were collected from patients suspected of scrub typhus in different discipline wards and intensive care units.

Inclusion criteria

All subjects with fever ≥38°C for less than 2 weeks, irrespective of age, gender, and socio-economic background were included.

Exclusion criteria

Those presenting with infection of known origin other than scrub typhus and absence of fever (≤ 38°C) were excluded.

Technical information

All study participants who fulfilled the inclusion criteria were included in the study, amounting to 3579 participants. The patient's case records were analysed for clinical manifestations and demographic characteristics. All 3579 serum samples received were subjected to the automated enzyme-linked immunosorbent assay (ELISA, with a cut-off of optical density, or OD, >0.5) using Scrub Typhus Detect™ Kit, InBios International, USA, which consists of the recombinant p56kDa type-specific antigens of *O. tsutsugamushi* Karp, Kato, Gilliam and TA 716 strains according to the manufacturer's instructions. Furthermore, those serum samples that were IgM-positive considered as scrub typhus-positive cases. All information about symptoms, medical history, and authorisation (obtained from the healthcare provider) was collected for serological assessment following the guidelines outlined in the Case Study and Case Record Form (CRF). The current investigation constitutes a retrospective analysis without direct engagement in patient care interventions. The specimens procured for diagnostic procedures were delivered to the laboratory after obtaining approval from the individuals for diagnosis. Patient confidentiality remained intact throughout the entire process.

Statistical analysis

The data was collected in a Microsoft Excel spreadsheet and was assessed utilizing Epi-Info software (version 3.5.1, Centre for Disease Control and Prevention, Atlanta, GA, USA). Descriptive statistics were applied to assess the outcomes. Continuous data was presented using mean and standard deviation, whereas

categorical data was represented with the help of ratios and percentages. Statistical comparison of categorical data involved chi-square tests, with a significance level set at P<0.05.

3. RESULTS

In the current study, 3579 serum samples were tested irrespective of age, gender, or socio-economic status, of which 235 (6.57%) were found to be IgM positive for *O. tsutsugamushi* using the automated ELISA and Scrub Typhus Detect™ Kit (IgM), InBios International, USA, indicating a diagnosis of scrub typhus febrile illness. A ratio of 2.012:1 was seen between males and females. It was statistically significant (p-value <0.005). Most scrub typhus-positive patients were reported from the 21 to 40 age group (31.49%, n=74) shown in [**Table 1**]

Table 1: Gender and age wise distribution of scrub typhus positive patients (n=235)

AGE GROUP	SCRUB TYPHUS (POSITIVE) (N=235)*		TOTAL** (%)
(years)	MALE (%)	FEMALE (%)	
0-20	33 (62.26)	20 (37.35)	53 (22.55)
21-40	52 (70.27)	22 (29.72)	74 (31.49)
41-60	39 (62.90)	23 (37.10)	62 (26.38)
>60	33 (71.73)	13 (28.27)	46 (19.57)
TOTAL	157 (66.81)	78 (33.19)	235 (100)

*The P-value for gender comparison using the paired sample t-test is <0.0000001.

**Median (IQR)- 35.5 (36); maximum, 83 years; minimum, 9 months [age group]

Coefficient of variance: 60% (showing large disparity with mean, leading to nearly equal distribution of scrub typhus positive cases among the given ranges)

Population trend

Among the 235 positive cases, a notable increase in urban cases infected with scrub typhus was observed compared to rural areas [**Table 2**]. In both rural and urban cases

Table 2: Population distribution in scrub typhus positive (n=235)

AREA OF RESIDENCE	SCRUB TYPHUS POSITIVE (%) (n=235)	OCCUPATION (%)		
		Farmers	Self-employed/ students/others	Housewife/ Unemployed
Rural	134 (57.02)	73(54.48)	40(29.86)	21(15.67)
Urban	101 (42.97)	30(29.70)	46(45.54)	25(24.75)
Total	235 (100)	103(43.83)	86(36.60)	46(19.57)

Clinical features

Diverse non-specific clinical features, including headache (59.57%, n=140), dermatological eruptions like maculopapular rashes (20%,n=47), and noticeable gastrointestinal disturbances such as diarrhoea & vomiting (11.91%, n=28) were also seen. A range of symptoms, particularly specific to specific organ systems, were primarily found, such as polyarthralgia (41.28%, n=97), lymphadenopathy(30.21%, n=71), hepatomegaly (14.89%,n=28), and splenomegaly (6.81%, n=16). Seizure (4.68%, n=11) emerged as the solitary neurological symptom documented in the present study. The peculiar sign of scrub typhus, known as eschar (2.55%, n=6), was noted in a limited subset of the population. Men demonstrated a noteworthy correlation with the manifestation of scrub typhus-related clinical symptoms in comparison to their female counterparts (p<0.005) shown in [**Table 3**].

Table 3: Gender distribution of clinical manifestation in scrub typhus-positive patients

CLINICAL MANIFESTATIONS	POSITIVE (%)	MALE (%)*	FEMALE (%)*
Headache	140 (59.57)	66(47.14)	74 (52.36)
Polyarthralgia	97 (41.28)	52 (53.41)	45 (46.39)
Lymphadenopathy	71 (30.21)	50 (70.42)	21 (29.58)
Maculopapular Rashes	47 (20)	29 (61.70)	18 (38.30)
Hepatomegaly	35 (14.89)	25 (71.43)	10 (28.57)
Diarrhea & Vomiting	28 (11.91)	10 (35.71)	18 (64.28)
Splenomegaly	16 (6.81)	9 (56.25)	7 (43.75)
Seizures	11 (4.68)	6 (54.54)	5 (45.45)
Eschar	6 (2.55)	4 (66.67)	2 (33.34)

*The P-value (two tailed) for gender comparison using the sample t-test (with unequal variance) is 0.000956 and chi-square is 28.0326.

Seasonal trend

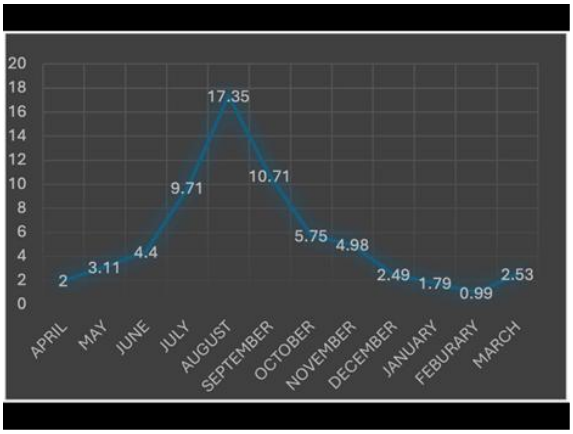

Figure 1: Monthly trend of scrub typhus positive patients (x-axis: month, y-axis: percentage of scrub typhus positive monthly)

A distinct seasonal fluctuation of scrub typhus fever is observed, exhibiting a notable increase

from July (9.71%,n=40) to September (10.71%,n=44), reaching its pinnacle in August, followed by a substantial decline over the subsequent four months, spanning from October to January, thus forming the typical profile resembling a hill shown in [**Figure 1**].

4. DISCUSSION

Scrub typhus, which is caused by *O. tsutsugamushi*, represents a significant yet neglected zoonotic disease spread by vectors with a known extensive geographical range. The intricacies of the ecology of the disease are multifaceted and lacking in comprehension, hindering the discourse on interventions for public health [8]. In India, scrub typhus is a common zoonotic disease, particularly disseminated in the eastern region.

The current study reported 235 (6.67%) scrub typhus-positive cases out of 3579 serum samples. Previous studies in India revealed seroprevalence of scrub typhus varying from 6% to 25% [9-11]. Specific reports from the eastern part of the country, especially from Odisha, documented higher seroprevalence of scrub typhus [12, 13]. With the decline in malaria and filarial cases in Odisha, other zoonotic causative agents of pyrexia of unknown origin, such as scrub typhus, leptospirosis, etc., have contributed to increasing clinical burden in recent years. The phenomenon is increasingly manifesting in urban settings and should no longer be perceived solely as an issue confined to rural regions. In this study, the rural area (57.06%, n=134) was affected slightly more than the urban regions (42.09%,n=101), and male predominance was observed. The explanation for this shifting trend to urban regions could be increased transmission by domestic rodents, specific diagnoses like IgM ELISA availability, and changes in empirical antimicrobial prescription. The male is more exposed to outdoor activities than their female counterpart, which can be the possible reason for this study's male preponderance 14, 15].

The present study documented most of the scrub typhus-positive patients in the younger adult age group (21-40 years; 74, 31.49%) that were predominantly male. The median age was observed to be 35.5 years. Parai *et al.,* (2023) [16] and Kader *et al.,* (2016) [17] reported similar results of seropositive patients belonging to relatively younger age groups, i.e., 21-40 years (53% & 30 %, respectively). Young adults being the most actively working age group, were more majorly affected due to continuous exposure to the outside environment, especially in rural areas, such as working in the farms and close contact with vectors involved in harbouring chiggers' mites. A significant proportion of the pediatric age group (22.55%, n=53) were also affected. This indicates that the habitat of the chiggers has progressively moved closer to our homes, emphasizing the need for essential interventions to address the underlying issue [18].

Scrub typhus remains underdiagnosed and untreated due to a lack of specific signs & symptoms. The present study documented various other non-specific symptoms, of which headache (59.57%, n=140) was the most predominant one, followed by maculopapular rashes (20%, n=47) and diarrhoea & vomiting (11.91%, n=28). Similarly, Jyothi *et al.,* (2015) [19], Bal *et al.,* (2021) [13]. and Devasagayam *et al.,* (2021) [20] extensive review across India showed headache (53.54%, 48.30%; 18.27% respectively) being most common general symptom followed by nausea & vomiting and rashes. These vague symptoms are also associated with diseases like leptospirosis, dengue, and malaria, making the diagnostic algorithm more difficult. Differentiating it from other prevalent diagnoses necessitates specialized and definitive tests, careful clinical evaluation, and a thorough patient medical background.

Eschar, the pathognomonic sign of scrub typhus, was found rarely (2.55%, n=6), but it didn't rule out the scrub typhus diagnosis. An eschar represents a necrotic skin lesion that develops at the location where an infected chigger, the larval stage of trombiculid mites (Leptotrombidium spp), punctures the skin during its feeding process. This typically occurs in warm, humid regions with pressure due to clothing, but it can also appear in atypical areas such as the ear lobes, wrist, and forearm. Vigilant clinical suspicion with other associated signs and symptoms were

considered and sent for microbiological IgM ELISA investigations. The presence of eschar exhibits significant variability and has the potential to remain undetected by both the patient and the clinician.[13] Specific symptoms associated with scrub typhus, for example, lymphadenopathy (30.21%, n=71), polyarthralgia (41.28%, n=97) and hepatomegaly (14.89%, n=37) were also observed. Lymphadenopathy was observed as a prevalent symptom in the regions of northern, southern, and eastern India [10, 12]. Hepatomegaly and splenomegaly were identified as distinctive symptoms within the organ system of patients testing positive for scrub typhus [10, 12, 21]. The only neurological symptom found in the present study was a seizure, which was observed most commonly in the paediatric age group. Kalita *et al.,* (2016) reported a higher percentage of seizures in children suffering from acute encephalitis caused primarily by scrub typhus infection. Seizure is associated with poor outcomes but not significantly to mortality in such situations [22].

Our current investigation observed a notable prevalence of scrub typhus during the monsoon and post-monsoon periods. In contrast, the positive cases were limited during the winter and summer. The pinnacle duration was between August (17.35%, n=71) and September (10.71%, n=44). There was a substantial correlation between the amount of scrub typhus in our vicinity and the precipitation of the surrounding area, suggesting an escalated presence of mites during the monsoon period. The Regional Medical Research Centre (RMRC), Bhubaneswar, an institute of ICMR, conducted a study in Keonjhar, Odisha, that documented a substantial prevalence (39.7%) of scrub typhus among children from July to September, which is traditionally recognised as the peak season for spread of various other vector-borne diseases such as dengue, malaria, and leptospirosis [23]. Several previous studies have elucidated the surge of cases in the monsoon season compared to the summer months, attributing it to the heightened disease transmission by mites during these rainy intervals [21-24].

Limitation

The current study is subjected to a few limitations. One such limitation includes only performing the IgM ELISA test and being unable to perform a PCR test for further confirmation. Furthermore, we could not track all scrub typhus positive prognosis due to the retrospective nature of the case study.

5. CONCLUSION

In conclusion, the investigation comprehensively explains the demographic and clinical manifestation of scrub typhus in eastern India. The distinct seasonal patterns identified in the analysis provide valuable insights for targeted surveillance and control strategies. Despite challenges in diagnosis and the absence of specific signs, the study emphasises the significance of early recognition and prompt treatment to mitigate the impact of scrub typhus on affected populations. With the disease's expansion into urban areas and its association with diverse clinical manifestations, this research underscores the urgency for sustained research efforts and proactive public health strategies to effectively address this infectious ailment's resurgence. This study aims to steer and motivate forthcoming research initiatives and policy actions, advocating a collective approach to tackle the evolving challenges posed by scrub typhus in Odisha.

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Ethical consideration

All information about symptoms, medical history, and authorisation (obtained from the healthcare providers) was collected for serological assessment following the guidelines outlined in the Case Study and Case Record

Form (CRF). The specimens procured for diagnostic procedures were delivered to the laboratory after obtaining approval from the individuals for diagnosis. Patient confidentiality remained intact throughout the entire process. The review committee approval was received from the institute via **letter no.: IMS/SRC/789/2025 dated 08/04/2025.** As the current investigation constitutes a retrospective analysis without direct engagement in patient care interventions, Ethical committee approval was exempted by the parent institution.

Conflicts of interest
Nil

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Nil.

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